REMARKS

Claims 1-4, 6-8, 10-13, 15-16, 18-49 and 52-59 are pending. Claims 25-45 stand withdrawn. Claim 20 is amended herein. Support for the claim amendment can be found throughout the specification and claims as filed. Applicants reserve the right to file at least one continuation directed to any subject matter canceled herein. Applicants respectfully request the Examiner to reconsider and withdraw the outstanding rejections in view of the foregoing amendments and the following remarks.

Claims 1-3, 6-8, 10-13, 15-16, 18-24, 46-49 and 52-59 stand rejected under 35 U.S.C. § 112, first paragraph as purportedly lacking enablement.

The Office acknowledged that the specification enables a method of promoting remyelination of nerve cells or reversing paralysis in a multiple sclerosis (MS) subject. However, the Examiner indicated that a person of ordinary skill in the art would not have predicted that anti-VLA-4 antibodies would be useful for treating other clinical disorders involving demyelination as recited in claim 3 or "reversing paralysis" in subjects having the conditions recited in claim 47. Applicants disagree.

Exhibit 1 entitled "Natalizumab Significantly Increases the Cumulative Probability of Sustained Improvement in Physical Disability" Munschauer et al. (setting forth data from the AFFIRM study) demonstrates that not only does the specification enable a method of promoting remyelination, it also demonstrates that the specification enables a method that reverses paralysis in subjects having

the conditions recited in claim 47. See in particular Figures 1-4 which present data on the sustained improvement in physical disability in the patients and the "Conclusions" which recites :

> "This analysis provides the first evidence that natalizumab is associated with a significant improvement in functional outcome, rather than only slowing or preventing progression of disability, in a group of patients with relapsing MS."

This post hoc analysis is of the AFFIRM study population. The methods of the AFFIRM study was published previously in Polman et al. the New England Journal of Medicine (2006) 354(9):899-910 also enclosed. This data illustrates that natalizumab is effective in promoting remyelination and reversing paralysis in demyelinating diseases.

In view of the foregoing remarks, Applicants request that the rejection of claims 1-3, 6-8, 10-13, 15-16, 18-24, 46-49 and 52-59 under 35 U.S.C. § 112, first paragraph be withdrawn.

Claims 1-4, 6-8, 10-13, 15-16, 18, 46-49 and 52-58 stand rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over WO 00/15247. Claims 1-4, 6-8, 10-13, 15-16, 18, 46-49 and 52-56 stand rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over U.S. Patent No. 5,840,299. Claims 1-4, 19-21, 49, 57 and 58 stand rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over WO 00/15247 in view of U.S. Patent No. 6,284,473. Claims 1-4, 19-20, 22-23, 49, 57 and 59 stand rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over WO 00/15247 or U.S. Patent No. 5,840,299, each in view of U.S. Patent No. 6,753,135. Claims 1-4, 19-21, 57 and 58 stand

rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over U.S. Patent No. 5,840,299 in view of U.S. Patent No. 6,602,885.

Specifically, the Office states that the primary references, the '247 publication and the '299 patent, teach treatment of multiple myeloma (MM) and MS, respectively, using anti-VLA-4 antibodies. The Office acknowledges that these publications do not explicitly teach the remyelination of nerve cells or the reversal of paralysis. However, the Office argues that because the treatment methods are the same, the referenced methods inherently result in remyelination of nerve cells and reversing paralysis. The Office also acknowledges that the publications do not explicitly teach chronic administration weekly or monthly over a period of at least six months or a year.

Applicants submit that their teachings for chronic administration of natalizumab has displayed unexpected benefits in the treatment of demyelinating conditions. Exhibit 1 demonstrates that the chronic administration of natalizumab over time not only promotes remyelination, but it reverses paralysis in subjects. None of the cited references disclose these benefits of chronic administration. Thus, not only do the cited references fail to disclose chronic administration of anti-VLA-4 antibodies, but the references fail to disclose the reduction of demyelination caused by demyelinating disease states. Accordingly, at the time invention was made one of ordinary skill in the art would not have had an expectation of successfully achieving the effect of reduction of demyelination, and accordingly would not have combined the elements of the cited references to arrive at the present invention. Furthermore,

there is no motivation to combine the secondary references cited by the Office with WO 0015247 and U.S. Patent No. 5,840,299 and even if combined, the combination fails to resolve the differences between the primary references, the '299 patent and the '247 publication, and the claims in issue.

In view of the foregoing remarks, Applicants request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. § 103.

If there are any questions regarding this response or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket # 103930.B080061).

Respectfully submitted,

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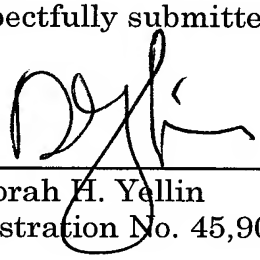

Deborah H. Yellin
Registration No. 45,904

CROWELL & MORING, LLP
Intellectual Property Group
P.O. Box 14300
Washington, DC 20044-4300
Telephone No.: (202) 624-2500
Facsimile No.: (202) 628-8844
DHY/hk

Attachments